REMARKS

Claims 52 and 53 are pending in the subject application. By this Amendment, applicants have amended claim 52 in a manner which is fully supported by the specification as filed at, *inter alia*, page 3, lines 3-6; page 15, lines 8-16; page 18, line 28 to page 19, line 18; page 19, lines 27-30; page 20, lines 25-27; page 21, lines 13-14; page 34, line 34 to page 35, line 9; page 35, lines 20-24; page 36, lines 8-30; and line 32 to page 37, line 8; page 38, lines 32-35; page 39, line 5 to page 40, line 2. Thus, these amendments do not raise any issue of new matter. Accordingly, applicants respectfully request that the Examiner enter this Amendment. Upon entry of this Amendment, claims 52 and 53, as amended, will be pending.

The Claimed Invention

This invention provides an isolated peptide (i) encoded by a nucleic acid molecule of at least 30 nucleotides in length having a sequence which constitutes a portion of the sequence set forth in SEQ ID NO:14, and (ii) which binds to an antibody in a binding reaction that is determinative of a herpesvirus associated with Kaposi's sarcoma. The invention also provides a composition comprising the instant isolated peptide and a carrier.

Rejections Under 35 U.S.C. §112, First Paragraph

Written Description

The Examiner rejected claims 52 and 53 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner also stated that this rejection is maintained for the reasons set forth in the previous Office Action.

In response to the Amendment filed June 25, 2004, the Examiner stated that applicants' arguments have been fully considered but are not persuasive. Concerning the Written Description rejection, the Examiner summarized applicants' grounds of traversal as follows:

1. Applicants argue that "it would be routine to identify a large number of such $\geq$ 30-nt sequences from the nucleotide sequence of SEQ ID NO:14, based on the specification," and that by using tools in the prior art, "one skilled in the art could easily determine which peptides encoded by such $\geq$ 30-nt sequences uniquely define a herpesvirus associated with Karposi's sarcoma" (citing, for example, page 6, the top of the third paragraph of applicants' response).

2. Applicants assert that the provision of the complete nucleotide sequence of SEQ ID NO:14 is sufficient disclosure of a relevant identifying characteristic, i.e., structure, to show that applicants were in possession of the claimed genus (citing, for example, page 6, the bottom of the third paragraph of applicants' response).

3. Applicants argue that the prior art discloses homology search tools such as BLAST, which overcome the deficiencies in the description of the claimed invention. The Examiner stated that applicants' contention, therefore, is that the Office's statement that the prior art does not provide teachings regarding sequences within SEQ ID NO:14 that are unique to a herpes virus associated with Karposi's sarcoma

> are without merit (citing, for example, page 7, top paragraph of applicants' response).

The Examiner stated that applicants' arguments are not found convincing for the following reasons:

First, the Examiner stated that the ability of the skilled artisan to identify $\geq$ 30-nt sequences of SEQ ID NO:14 that uniquely define a herpesvirus associated with Karposi's sarcoma is not the issue that is raised in a Written Description rejection. The Examiner also stated that the standard for Written Description is not that the invention must be identifiable, but rather that it must be described. The Examiner further stated that, by definition, if the skilled artisan must identify the sequences that are claimed, the sequences cannot be described; otherwise there would be no need to identify these sequences. The Examiner additionally stated that what has been described is SEQ ID NO:14 but that there is no description of which sub-sequences meet the functional limit of being "unique" to a herpesvirus associated with Karposi's Sarcoma. The Examiner also stated that as such, applicants' argument that the sequences could be identified does not indicate that those sequences were described, and the arguments cannot overcome the rejection.

In response, applicants respectfully traverse this rejection.

Applicants note that the legal standard for an adequate written description, as set forth in 35 U.S.C. §112, first paragraph, is that:

> [t]he specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with

> which it is most nearly connected, to make and use the same ...

According to M.P.E.P. §2163.02, the fundamental factual inquiry in testing the adequacy of a written description is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed (citing, for example, *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)).

Applicants maintain that the specification satisfies the written description requirement. In this regard, applicants note that claim 52, as amended, recites an isolated peptide encoded by a nucleic acid molecule of at least 30 nucleotides in length within the sequence set forth in SEQ ID NO:14, and which binds to an antibody in a binding reaction that is determinative of a herpesvirus associated with Kaposi's sarcoma (KSHV). Applicants note that the specification discloses the sequence of the KSHV ORF21 (thymidine kinase gene) as set forth in SEQ ID NO:14 (see, *inter alia*, page 20, lines 25-27 and page 21, lines 13-14). The specification also discloses an isolated DNA molecule which is at least 30 nucleotides in length and which uniquely defines a KSVH (see page 3, lines 3-6; page 19, lines 27-30), and DNA molecules encoding fragments of antigenic polypeptides (page 34, lines 1-3). Further, the specification discloses an isolated peptide which is encoded by at least a portion of a nucleic acid molecule with a sequence as set forth in, *inter alia*, SEQ ID NO:14. The specification also discloses an antibody that binds to said peptide (page 35, lines 20-24). Applicants note the disclosure that the isolated peptide may specifically bind to an antibody in a binding reaction which is determinative of the presence of the herpesvirus of the invention in the presence of a heterogeneous population of proteins and other biologics, including viruses other than the herpesvirus (page 18, line 28 to page 19, line 1).

In addition, the specification provides details of a variety of immunoassay formats which may be used to select antibodies specifically immunoreactive with a protein (page 19, lines 2-18). As disclosed in the specification, immunoassays can also be used to detect specific peptides of KSHV (page 38, lines 32-35). Methdods to select specific peptides encoded by isolated DNA molecules in order to generate antibodies are further disclosed (page 36, lines 8-30), as are methods for preparing antibodies (page 36, line 32 to page 37, line 8; page 39, line 5 to page 40, line 2).

In response to the Examiner's assertion that, by definition, if the skilled artisan must identify the sequences that are claimed, the sequences cannot be described, applicants note that claim 52, as amended, recites an isolated peptide which is defined, in part, by a specific antibody binding reaction. Applicants maintain that, given the above-cited disclosures in the specification and the high level of skill in the art, satisfying the written description requirement does not require a listing of individual peptides encoded by ≥ 30-nucleotide-long portions of SEQ ID NO:14 which meet the claim limitations. Applicants maintain further that the separating out and listing of these individual peptides demands a degree of description above and beyond that which is minimally required. Applicants respectfully submit, therefore, that based on the disclosures in the subject specification, one skilled in the art would recognize that applicants were in possession of the claimed invention at the time of filing the application.

Second, the Examiner stated that what is described in the instant specification with regard to the claims is SEQ ID NO:14 and there is not even an assertion that this sequence is "unique." The Examiner also stated that, contrary to what applicant suggests, this does not mean that all "unique"

polypeptides encoded by sub-sequences/fragments within SEQ ID NO:14 are described, as the Merriam-Webster dictionary defines "unique" as "being the only one." The Examiner asserted that the inclusion of the term "unique" in the claim thus confers a functional limitation on the claimed sequences whereby no claimed sequence can exist anywhere else, ever. The Examiner also stated that this is not a question of novelty at the time of filing since in order for something to maintain the functional characterization of "unique," it must never be duplicated.

The Examiner stated that, for instance, at the time of filing, the skilled artisan might guess that any such polypeptide encoded by any portion of SEQ ID NO: 14 was "unique," there being no guidance in the specification to dictate which potential polypeptides were or were not unique. The Examiner also stated that the skilled artisan might choose the polypeptide corresponding to amino acids 257-266 (YLEGVMGVGK) of the protein encoded by SEQ ID NO:14. The Examiner noted that while at this time of filing, the sequence met the functional limitation of being "unique," an identical polypeptide was later identified within a rhesus macaque rhadinovirus (citing, for example, Searles *et al.* (1999) J. Virol. 73: 3040-3053; specifically the EMBL entry AF083501, and more specifically sub-entry AAD21347.1). The Examiner also stated that this new sequence, while not undermining the novelty of the identical sequence within SEQ ID NO:14, does undermine its "uniqueness."

The Examiner stated that a similar situation exists for the polypeptide corresponding to amino acids 263-272 (GVGKSTLVNA) of the protein encoded by SEQ ID NO:14. The Examiner also stated that at the time of filing, the sequence met the functional limitation of being "unique." The Examiner further stated that, however, an identical polypeptide was later identified within the *V. parahaemolyticus* genome (citing, for example, Makino *et al.*

[2003] Lancet 361: 743-749; entire document, specifically the EMBL entry AP005089, and more specifically sub-entry BAC62972.1). The Examiner additionally stated that the instant specification does not describe what other potential polypeptides have a structure (i.e., a sequence) that will necessarily meet the functional limitation of being "unique." The Examiner further stated that it should be clear that this is NOT an art issue, but rather an issue of meeting the functional limitation of "unique," and how the instant specification does not describe structural elements (i.e., sequences) that meet the functional limitation.

The Examiner stated that the point here is that the skilled artisan has no idea as to what is being claimed in the instant claims. The Examiner further stated that this is because there is no distinct description as to what polypeptides meet the limitation of being "unique." The Examiner asserted that while at the time of filing the aforementioned polypeptides would have fit within the boundaries of the claimed invention, it is clear that they no longer meet the limitation of being "unique" and can longer be claimed. The Examiner also stated that with regard to the claims at hand, there is thus no description of what peptides will have a specific structure that necessarily meets the limitation of being "unique" (as opposed to novel).

In response, applicants respectfully respectfully point out that claim 52, as amended, does not recite the term "unique." Applicants maintain, therefore, that the Examiner's remarks regarding the term "unique" are moot.

Third, the Examiner stated that the BLAST program in and of itself does not describe anything regarding the protein encoded by SEQ ID NO:14. The Examiner also stated that it thus cannot satisfy a description of "unique" polypeptides encoded by SEQ ID NO:14. The Examiner further stated that the ability to identify

a protein that falls within the scope of the claim does not satisfy the requirement of that protein having been described in terms of a structure-function relationship.

In response, applicants note that claim 52, as amended, does not require use of the BLAST program. Accordingly, applicants respectfully submit the Examiner's remarks regarding the BLAST program are moot.

The Examiner stated that, in conclusion, one cannot rely on the ability to identify a polypeptide as "unique" in order to meet the written description requirement. The Examiner further stated that if a polypeptide must be identified, then it cannot be described in terms of a structure-function relationship. The Examiner also stated that, furthermore, even if a particular polypeptide was selected and determined to be "unique" at a particular time (for example, the time of filing), this does not satisfy the functional limitation of being "unique." The Examiner asserted that this is demonstrated above where certain polypeptides encoded by SEQ ID NO:14 were "unique" at the time of filing, but no longer meet the functional limitation of being "unique." The Examiner concluded that, as such, the Written Description rejection is maintained.

In response, applicants note again that independent claim 52, as amended, and claim 53 which depends from it, do not require the identification of a "unique" polypeptide, and that, therefore, the Examiner's above remarks are moot.

For the reasons set forth above, maintain that the pending claims, as amended, satisfy the written description requirement of 35 U.S.C. §112, first paragraph.

Enablement

The Examiner also rejected claims 52 and 53 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner further stated that this rejection is maintained for the reasons set forth in the previous Office Action.

The Examiner stated that applicants' arguments filed June 25, 2004 have been fully considered but are not persuasive. The Examiner summarized applicants' grounds of traversal concerning the Enablement rejection as follows:

1. Applicants again argue that the skilled artisan would be able to readily identify peptides encoded by fragments of SEQ ID NO:14 that are unique to a herpesvirus associated with Karposi's sarcoma (citing, for example, page 9, the last paragraph of applicants' response).

2. Applicants assert that the "mere possibility of the existence of an unidentified nucleic acid sequence cannot be used to deny the demonstrated uniqueness of any given sequence" (citing, for example, page 10, the second paragraph of applicants' response).

The Examiner stated that applicants' arguments are not found convincing for the following reasons.

First, the Examiner asserted that similar to the Written Description rejection, the ability to identify a polypeptide is

not the standard for meeting the Enablement requirement. The Examiner stated that in order for the Enablement requirement to be met, the skilled artisan must be able to make and use the claimed invention. The Examiner further stated that, however, if the invention has yet to be identified, one of skill cannot make the invention. The Examiner concluded that applicants' arguments are thus not convincing.

Applicants respectfully traverse this rejection.

Applicants note that this ground of rejection is essentially predicated on the assertion that the specification does not satisfy the written description requirement, rather than on an independent assessment of whether one skilled in the art would be able to make and use the claimed invention. Applicants incorporate by reference the arguments made hereinabove that the written description requirement is in fact satisfied.

Applicants note also that the legal standard for the enablement requirement is provided in 35 U.S.C. §112, first paragraph, as quoted above. The requirements for enablement are further explicated in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988):

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. ... The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed. The term "undue experimentation" does not appear in the statute, but it is well established that enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations. ... Factors to be

> considered in determining whether a disclosure would require undue experimentation have been summarized by the Board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. (emphasis added, footnotes omitted)

Applicants note that not all the *Wand* factors must necessarily be considered: "... it is not necessary that a court review all of the *Wands* factors to find a disclosure enabling. They are illustrative, not mandatory. What is relevant depends on the facts ..." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991).

Applicants maintain that in the instant application, consideration of the *Wands* factors clearly indicate that the claimed invention is enabled by the specification as filed.

For example, applicants maintain that little experimentation is necessary, and such experimentaion as required is routine production of isolated peptides and antibody binding assays. Applicants note that the specifcation provides abundant guidance in the required methodologies, citations to which are provided hereinabove. Applicants note further that the level of skill in the molecular biological arts is very high. Finally, applicants note that it is highly predictable, using the disclosures of the subject application, to isolate peptides encoded by portions of SEQ ID NO. 14 of at least 30 nucleotides in length, which peptides bind to an antibody in a binding reaction that is determinative of KSHV. Thus, applicants maintain that one skilled in the art could readily practice the invention claimed herein without undue experimentation by using the disclosures of the subject application. Accordingly, applicants respectfully

submit that the specification as filed enables the claimed invention.

Second, the Examiner stated that contrary to the assertion that the "mere possibility of the existence of an unidentified nucleic acid sequence cannot be used to deny the demonstrated uniqueness of any given sequence," the Office has demonstrated that the uniqueness of any sequence can be questioned. The Examiner asserted that this is clear from the fact that at least two polypeptides of 10 amino acids or longer (both of which are within the protein encoded by SEQ ID NO:14) undermine the functional limitation of "unique" in the instant case. The Examiner stated that because the instant claims have been written to include the functional limitation of "unique," the claims must meet that limitation in terms of enablement. The Examiner further stated that this means that the skilled artisan must be able to make a polypeptide encoded by SEQ ID NO:14 that maintains its "uniqueness." The Examiner also stated that, however, this cannot be done in the instant case, because the skilled artisan cannot make a protein that is necessarily "unique," as evidenced by the examples presented in the response to arguments concerning the Written Description rejection. The Examiner additionally stated that this is because there is no guidance in the specification as to which polypeptides are considered "unique," and the prior art provides no information on the subject.

The Examiner again asserted that the ability to identify a polypeptide does not satisfy the enablement requirement of "to make and use." The Examiner further asserted that identifying a polypeptide that is "unique" at one point in time does not necessarily meet the limitation of unique. The Examiner stated that this is because that polypeptide may be present in another polypeptide which, upon its sequencing, negates the functional ability of the polypeptide to meet the limitations of the claim.

The Examiner noted that this is indeed already true in the instant case concerning at least the polypeptides YLEGVMGVGK and GVGKSTLVNA (which are encoded by sub-sequences within SEQ ID NO:14). The Examiner stated that these polypeptides cannot be considered to meet the limitations of the instant claims because they have been found in a virus other than a herpesvirus associated with Karposi's sarcoma. The Examiner concluded that the skilled artisan would thus be left to question which polypeptides can be made that do meet the limitations of the claimed invention, given the limited guidance provided by both the instant specification and the state of the art.
In response, applicants respectfully traverse.

Applicants note again that claim 52, as amended, and dependent claim 53 do not recite the term "unique." Applicants maintain, therefore, that the Examiner's above remarks are moot.

Conclusion

In view of the arguments set forth above, applicants submit that the Examiner's rejections made in the September 16, 2004 Final Office Action have been overcome. Applicants therefore respectfully request that the Examiner reconsider and withdraw these rejections, and earnestly solicit allowance of both claims pending in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
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